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Synthesis of Transition State Inhibitors for *N*-Riboside Hydrolases and Transferases

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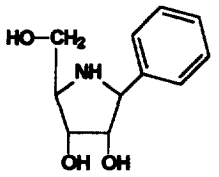
Abstract: A number of 1,4-dideoxy-1,4-imino-1-(S)-(substituted phenyl)-D-ribitols bearing aromatic OH, NH_2, NO_2, CO_2H and halogeno moieties, and a 3-pyridyl analogue have been synthesized. The key step is the condensation of aryllithium or aryl Grignard reagents with the imine **3**; derived from the protected 1,4-dideoxy-1,4-imino-D-ribitol **4**.

INTRODUCTION

Protozoan parasite infections are a major health problem world-wide with more than a million deaths per year resulting from malaria, trypanosomiasis and related protozoan infections[1]. A potentially useful feature that distinguishes protozoan parasites from their mammalian or insect hosts is the lack of a *de novo* pathway for purine biosynthesis[2]. The protozoa are required to salvage purines from the host for DNA and RNA synthesis. A family of nucleoside hydrolases is known to be present in such organisms[3,4] and nucleoside hydrolases have been implicated in the purine salvage pathway of the trypanosome *Crithidia fasciculata*[5,6]. Two distinct nucleoside hydrolases have been isolated from *Crithidia fasciculata*[5,6], and a third from *Trypanosoma brucei brucei*[7]. The enzymes differ in their substrate specificity and in their mechanisms of hydrolysis[8,9]. Such enzymes are not known to exist in mammalian cells[10], and their apparently specific role in the protozoa suggest they may be suitable targets for antibiotic design.

The nature of the transition state for nucleoside hydrolysis by the IU nucleoside hydrolase ("IU" because the favoured substrates are inosine and uridine) from *Crithidia*[5,10] has been characterized using kinetic

isotope effects and computational methods[11,12]. Nucleoside hydrolase inhibitors incorporating the 1,4-dideoxy-1,4-imino-D-ribitol structure, such as phenyl iminoribitol **1**[13] and the amidrazones **2**[14] have been synthesized, and these have allowed further transition state analysis of the nucleoside hydrolase.[15-17]



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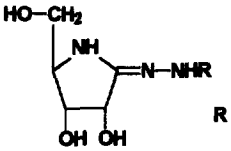
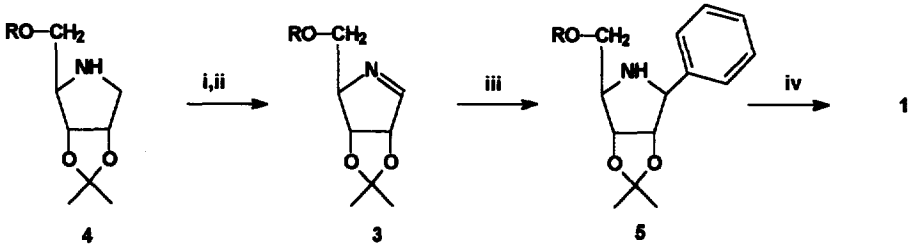


R = H, C_6H_5, p-I-C_6H_4
p-NO_2-C_6H_4

2

Enzymatic hydrolysis, or transfer, of 1-*N*-β-D-ribosyl moieties also occurs in the ADP-ribosylation of G-proteins catalyzed by bacterial toxins[18], the depurination reactions of plant toxins such as ricin[19], and in DNA repair reactions[20]. Although few of the reaction mechanisms of these processes have been characterized, it is proposed that the enzyme-stabilized transition states are similar to those for the nucleoside hydrolases[21,22]. Compounds **1** and **2** and derivatives thereof may therefore be useful for investigations with several of these important enzymes.

We present here the synthesis of a number of 1,4-dideoxy-1,4-imino 1-(S)(substituted phenyl)-D-ribitols to further explore the structure-activity requirements for inhibition of trypanosomal nucleoside hydrolases. Certain nucleoside hydrolases require activation of the base residue to effect glycosyl bond cleavage. The analogues described herein contain potential sites for protonation or for hydrogen bond formation with the enzyme. The biological results are being presented separately[9].



4 **3** **5**

R = ^{t}Butyldimethylsilyl

Reagents: i, NCS, pentane; ii, Li TMP, THF, -78°C; iii, PhMgBr; iv, 50% aq TFA.

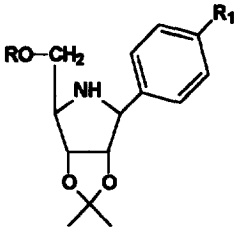
SCHEME 1

RESULTS AND DISCUSSION

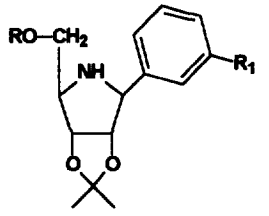
The phenyl iminoribitol **1** has been synthesized previously by the addition of phenylmagnesium bromide to imine **3** (Scheme 1), itself derived from the 1,4-dideoxy-1,4-imino-D-ribitol **4**, affording the 1-(S)-phenyl iminoribitol **5**[13]. The iminoribitol **4** is accessible from D-gulonolactone *via* a rather lengthy nine step process[13,23], but is nevertheless readily available on a multi-gram scale. We have utilized the same imine intermediate **3** and treated it with appropriate aryllithium or aryl Grignard reagents. An alternative approach has been recently reported[24] which involves aryllithium addition to a 2,3,5-*O*-protected-D-ribose, subsequent oxidation and then a double reductive amination.

Using 4-chlorophenylmagnesium bromide and 4-fluorophenylmagnesium bromide, the substituted phenyl iminoribitols **6** and **7** were obtained in 35% and 46% yield, respectively, from the iminoribitol **4**. 1,4-Dibromobenzene was selectively monolithiated (BuLi, -78°C) affording 4-bromophenyllithium which was allowed to react with imine **3** (THF, -78°C) to give the bromophenyl derivative **8**.

In order to prepare aniline derivatives, 3- and 4-bromoaniline were separately *N,N*-diallylated and the products treated with butyllithium, generating 3- and 4-*N,N*-diallylaminophenyllithium. These reagents were reacted *in situ* with imine **3** to give the protected aniline derivatives **9** and **10**. Similarly, *O*-^{t}butyldiphenylsilyl-4-bromophenol was treated with butyllithium and the lithiated aromatic was allowed to react with imine **3** affording the protected phenol **11**. Attempts to lithiate 3-bromopyridine by lithium- halogen exchange were

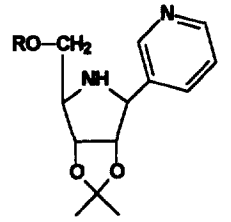


6 R_1 = Cl
7 R_1 = F
8 R_1 = Br
10 R_1 = $NAll_2$
11 R_1 = $OSiPh_2{}^tBu$
13 R_1 = COOH
29 R_1 = NH_2



R = ^{t}Butyldimethylsilyl

9 R_1 = $NAll_2$
28 R_1 = NH_2



12

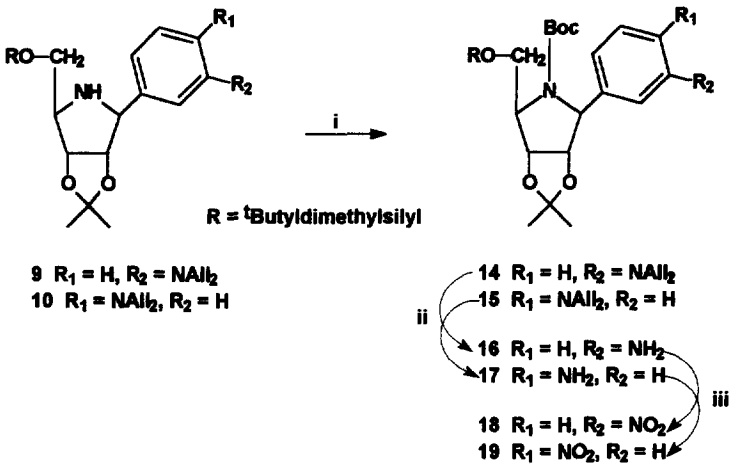
unsuccessful at -78°C, but at -100°C (THF, BuLi) the 3-lithiopyridine was generated, and on addition of imine **3** the pyridine **12** was obtained.

The 1-(S) stereochemistry of these adducts is assumed by analogy with the phenyl iminoribitol **5** which has been characterised by analysis of nOe's in its NMR spectrum[13].

The 4-bromophenyl iminoribitol **8** was treated with butyllithium (THF, -78°C) resulting in lithium-bromine exchange and the resulting aryllithium species was quenched *in situ* by CO_2 affording carboxylic acid **13**.

In order to prepare nitrophenyl derivatives, the anilines **9** and **10** were converted into ^{t}butyl carbamates **14** and **15** (Scheme 2) followed by de-*N*-allylation using Wilkinson's catalyst[25]. The resulting amines **16** and **17** were oxidised using oxone® (potassium peroxymonosulfate)[26] affording the nitrophenyl iminoribitols **18** and **19**.

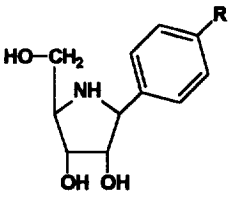
Deprotection of compounds **6-8**, **11**, **12**, **18** and **19** was achieved by acid hydrolysis followed by neutralisation of the product salts with base resin. This afforded the 1,4-dideoxy-1,4-imino-1-(S)-substituted phenyl)-D-ribitols **20-26**. The carboxylic acid **27** was obtained as the ammonium salt by acid hydrolysis of **13** followed by elution from acid resin with aqueous ammonia. Anilines **9** and **10** were first de-*N*-allylated using Wilkinson's catalyst to give **28** and **29** which were then subjected to acid hydrolysis followed by neutralisation with base resin affording the aminophenyl iminoribitols **30** and **31**.



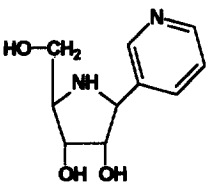
Reagents: i, $(Boc)_2O$, CH_2Cl_2, Et_3N; ii, $(Ph_3P)_3RhCl$, aq CH_3CN; iii, oxone, aq acetone.

SCHEME 2

The phenyl iminoribitol derivatives **20-27**, **30** and **31** are expected to provide useful information on the structure-activity requirements for inhibition of nucleoside hydrolases and to further extend understanding of the nature of the transition state of other *N*-ribosyl hydrolases and transferases.



20 R = Cl
21 R = F
22 R = Br
23 R = OH
26 R = NO_2
27 R = COOH
31 R = NH_2



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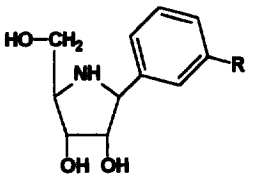

25 R = NO_2
30 R = NH_2

EXPERIMENTAL

N.m.r. spectra were recorded on a Bruker AC-300 instrument at 300 MHz or 75 MHz (^{13}C). In solvents other than D_2O, internal TMS was used as a reference. High resolution accurate mass determinations were performed on a VG70-250S mass spectrometer under chemical ionization conditions using isobutane or ammonia as the ionizing gas. Melting points were determined on a Reichert hot stage microscope and are uncorrected. Aluminium backed silica gel sheets (Merck or Reidel de Haen) were used for thin layer chromatography. Column chromatography was performed on silica gel (230-400 mesh, Merck). Optical rotations were measured on a Perkin Elmer 241 polarimeter. Chromatography solvents were distilled prior to use.

5-*O*-^{t}Butyldimethylsilyl-1,*N*-dehydro-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-D-ribitol (3)

A solution of 5-*O*-^{t}butyldimethylsilyl-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-D-ribitol **4** in pentane (15 ml / mmol.) was treated with *N*-chlorosuccinimide (1.3 equiv.) and the mixture was stirred at room temperature until complete conversion of the amine to the corresponding *N*-chloro compound as judged by t.l.c. (ethyl acetate : petroleum ether 1:4) (usually ~ 30 min.). The solids and solvent were removed and the residue was dissolved in dry tetrahydrofuran (15 ml / mmol.) and the solution was cooled to -78°C. A solution of 2,2,6,6-tetramethylpiperidine (1.5 equiv.) in dry tetrahydrofuran (5 ml / mmol.), previously treated with butyllithium (1.4 equiv.) at 0°C, was added very slowly dropwise over a period of 0.5 -1 h until no *N*-chloro compound could be detected by t.l.c. The resulting solution of title compound **3** was then used directly *in situ* in subsequent reactions. Material that was isolated by partitioning between chloroform and water and subsequent chromatography (EtOAc:petroleum ether 1:4) had ^1H n.m.r. (C_6D_6) δ 7.49(1H, d, H-1), 4.95(1H, d, H-2 or 3),

4.54(1H, d, H-2 or 3), 4.40(1H, br s, H-4), 3.57(2H, m, H-5,5'), 1.37 and 1.26(3H each, s), 0.83(9H, s), -0.09 and -0.10(3H each, s).

5-*O*-^{t}Butyldimethylsilyl-1-(S)-(4-chlorophenyl)-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-D-ribitol (6) To a solution of 1,*N*-dehydro-1,4-iminoribitol **3** derived from 0.25 g of iminoribitol **4** at -78°C was added dropwise 1.74 ml of a 2 M solution of 4-chlorophenylmagnesium bromide in dry ether. This mixture was stirred for 30 min at - 78 °C, allowed to warm up to r.t. and stirred for another 30 min. Ether (50 ml) and 5 % aq. NH_4Cl (30 ml) was added and the organic layer was washed twice with water and brine, dried with $MgSO_4$ and evaporated *in vacuo*. Final purification by flash chromatography (petroleum ether - ethyl acetate 10:1 + 1% triethylamine) afforded **6** as a colourless syrup (120 mg, 0.30 mmol, 35 % yield): $[\alpha]_D^{20}$ = -18.0 ° (*c* = 0.5 in CH_2Cl_2), HRMS calc. for $C_{20}H_{32}NO_3SiCl$: 397.1840; found: 397.1836. ^{1}H n.m.r. ($CDCl_3$) δ 7.25 (4H, m, Ar-H), 4.40 (1H, dd, J=5.5, 7.0Hz, H-2), 4.28 (1H, dd, H-3), 4.06 (1H, d, H-1), 3.76, 3.66 (1H each, dd, J = 10.2, and 5.5 or 3.7Hz, H-5,5'), 3.27 (1H, q, H-4), 1.49, 1.25 (3H each, s), 0.82 (9H, s), 0.08, 0.07 (3H each, s). ^{13}C n.m.r. δ 139.8, 133.0, 128.5, 127.8, 114.1, 87.4, 81.7, 67.2, 65.4, 63.8, 27.4, 25.8, 25.3, 18.1, -5.5.

5-*O*-^{t}Butyldimethylsilyl-1,4-dideoxy-1-(S)-(4-fluorophenyl)-1,4-imino-2,3-*O*-isopropylidene-D-ribitol (7) To a solution of 1,*N*-dehydro-1,4-iminoribitol **3** derived from 0.10 g of iminoribitol **4** at -78°C was added 1.0 ml of a 2M solution of 4-fluorophenylmagnesium bromide and the reaction mixture was stirred and allowed to warm to r.t. overnight, partitioned between toluene and water, filtered through celite, and the organic phase was dried ($MgSO_4$) and concentrated. Chromatography (petroleum ether, ethyl acetate 8:1) afforded title compound **7** (0.062 g, 46 %). HRMS calc. for $C_{20}H_{32}FNO_3Si$: 381.2136; found: 381.2142. ^{1}H n.m.r. ($CDCl_3$) δ 7.36(2H, dd, J = 8.5, 5.4 Hz, Ar-H), 7.02(2H, t, J = 8.6 Hz, Ar-H), 4.52(1H, dd, J = 7.0, 4.6 Hz, H-3), 4.41(1H, dd, J = 7.0, 5.4 Hz, H-2), 4.17(1H, d, J = 5.4 Hz, H-1), 3.86 and 3.77(1H each, dd, H-5,5'), 3.36(1H, q, J = 8.5, 4.6 Hz, H-4), 1.58 and 1.33(3H each, s, CH_3), 0.90(9H, s, ^{t}Bu), 0.08 and 0.07(3H each, s, CH_3). ^{13}C n.m.r. δ 162.2(d, $J_{C,F}$ = 245 Hz), 136.8(d, $J_{C,F}$ = 3 Hz), 128.1(d, $J_{C,F}$ = 8 Hz), 115.4(d, $J_{C,F}$ = 21 Hz), 114.3, 87.5, 81.9, 67.3, 65.5, 63.5, 27.6, 25.9, 25.4, 18.3, -5.4.

1-(S)-(4-Bromophenyl)-5-*O*-^{t}butyldimethylsilyl-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-D-ribitol (8) A solution of 4-bromophenyllithium [prepared by adding butyllithium (4.8 ml, 1.3 M, 6.24 mmol) slowly to 1,4-dibromobenzene (1.626g, 6.89 mmol) in tetrahydrofuran (15 ml) at -78°C] was added *via* cannula to a solution of 1,*N*-dehydro-1,4-iminoribitol **3** derived from 0.60 g of iminoribitol **4** at -78°C. After 1 h the reaction mixture was partitioned between chloroform and water and the organic phase was dried ($MgSO_4$) and concentrated. Chromatography (petroleum ether, ethyl acetate 8:1) afforded title compound **8** (0.512 g, 55 %). HRMS calc. for $C_{20}H_{32}{}^{79}BrNO_3Si$: 441.1335; found, 441.1336. ^{1}H n.m.r. ($CDCl_3$) δ 7.45 and 7.29(2H

each, d, J = 8.4 Hz, Ar-H), 4.46(1H, dd, J = 4.4, 7.0 Hz, H-3), 4.35(1H, dd, J = 5.3, 7.0 Hz, H-2), 4.13(1H, d, J = 5.3 Hz, H-1), 3.85 and 3.73(1H each, dd, H-5,5'), 3.35(1H, q, J = 4.4, 9.8 Hz, H-4), 1.58 and 1.32(3H each, s), 0.90(9H, s), 0.08 and 0.07(3H each, s). ^{13}C n.m.r. δ 140.7, 131.5, 128.2, 121.1, 114.1, 87.4, 81.8, 67.4, 65.5, 64.1, 27.5, 25.9, 25.4, 18.3, -5.4.

1-(S)-(3-*N,N*-Diallylaminophenyl)-5-*O*-^{t}butyldimethylsilyl-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-D-ribitol (9)

To a solution of 1,*N*-dehydro-1,4-iminoribitol **3** derived from 0.5 g of iminoribitol **4**, a solution of 3-*N,N*-diallylaminophenyllithium, [prepared from 3-*N,N*-diallylaminobromobenzene (880 mg, 3.49 mmol) in 10 ml dry ether, treated with 3.48 mmol butyllithium in hexane at -78 °C and kept at r.t. for 30 min] was added dropwise. This mixture was stirred for 30 min at - 78 °C, allowed to warm to r.t. and stirred for another 30 min. Ether (50 ml) and 5 % aq. NH_4Cl (30 ml) was added and the organic layer was washed twice with water and brine, dried ($MgSO_4$) and evaporated *in vacuo*. Final purification by flash chromatography (petroleum ether, ethyl acetate 10:1) afforded the title compound **9** as a light yellow syrup (463 mg, 1.01 mmol, 58 %): $[\alpha]_D^{20}$ = -13.5 ° (c = 2.1 in CH_2Cl_2), HRMS calc. for $C_{26}H_{42}N_2O_3Si$: 458.2964; found: 458.2978. ^{1}H n.m.r. ($CDCl_3$) δ 7.08 (1H, dd, Ar-H), 6.68 (1H, s, Ar-H), 6.63 (1H, d, Ar-H), 6.52 (1H, d, Ar-H), 5.75 (2H, m, CH=), 5.08 (4H, m, $=CH_2$), 4.40 (2H, m, H-2,3), 4.04 (1H, d, J = 4.0 Hz, H-1), 3.83 (4H, m, N-CH_2), 3.83, 3.69 (1H each, dd, H-5,5'), 3.22 (1H, ddd, H-4), 1.49, 1.25 (3H each, s), 0.82 (9H, s), 0.08, 0.07 (3H each, s). ^{13}C n.m.r. δ 148.8, 142.3, 134.0, 129.2, 116.0, 114.4, 113.9, 111.4, 110.6, 87.7, 81.7, 68.3, 65.7, 63.5, 52.7, 27.5, 25.9, 25.4, 18.3, -5.4.

1-(S)-(4-*N,N*-Diallylaminophenyl)-5-*O*-^{t}butyldimethylsilyl-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-D-ribitol (10)

A solution of 1,*N*-dehydro-1,4-iminoribitol **3** derived from 0.5 g of iminoribitol **4** was treated as described above in the preparation of **9**, but using 4-*N,N*-diallylaminophenyllithium in place of 3-*N,N*-diallylaminophenyllithium. Final purification was effected by flash chromatography (petroleum ether, ethyl acetate 10:1) affording **10** as a light yellow syrup (475 mg, 1.04 mmol, 60 %): $[\alpha]_D^{20}$ = -17.8 ° (c = 1.5 in CH_2Cl_2), HRMS calc. for $C_{26}H_{42}N_2O_3Si$: 458.2964, found: 458.2966. ^{1}H n.m.r. ($CDCl_3$) δ 7.12 and 6.59 (2H each, d, J = 8.7 Hz, Ar-H), 5.75 (2H, m, CH=), 5.08 (4H, m, $=CH_2$), 4.41 (1H, dd, J = 4.8, 7.0 Hz, H-3), 4.35 (1H, dd, H-2), 4.00 (1H, d, J = 5.0 Hz, H-1), 3.83 (4H, m, N-CH_2), 3.78, 3.68 (1H each, dd, J = 10.2 Hz, H-5,5'), 3.20 (1H, q, J = 4.5, 5.0 Hz H-4), 1.49, 1.25 (3H each, s), 0.82 (9H, s), 0.08, 0.07 (3H each,s). ^{13}C n.m.r. δ 148.1, 134.0 128.9, 127.4, 116.0, 113.9, 112.5, 87.8, 81.9, 67.6, 65.7, 63.6, 52.7, 27.5, 25.9, 25.4, 18.3, -5.4.

5-*O*-^{t}Butyldimethylsilyl-1-(S)-(4-^{t}butyldiphenylsiloxyphenyl)-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-D-ribitol (11)

A solution of 1,*N*-dehydro-1,4-iminoribitol **3** derived from 0.15 g of iminoribitol **4** was added *via* cannula at -78°C to a solution of 4-^{t}butyldiphenylsiloxyphenyl lithium [prepared by adding butyl lithium (1.21 ml, 1.3 M, 1.57 mmol) slowly to a solution of *O*-^{t}butyldiphenylsilyl-4-bromophenol (0.709 g, 1.72 mmol) in tetrahydrofuran (5 ml) at -78°C]. After 1 h the reaction mixture was partitioned between chloroform and water and the organic phase was dried ($MgSO_4$) and concentrated. Chromatography (petroleum ether, ethyl acetate 6:1) afforded title compound **11** (0.203 g, 63 %). HRMS calc. for $C_{36}H_{51}NO_4Si_2$: 617.3357; found: 617.3360. ^{1}H n.m.r. ($CDCl_3$) δ 7.66-7.63(4H, m, Ar-H), 7.38-7.26(6H, m, Ar-H), 7.05 and 6.67(2H each, d, J = 8.6 Hz, Ar-H), 4.39(1H, dd, J = 4.8, 7.1 Hz, H-3), 4.31(1H, dd, J = 5.2, 7.1 Hz, H-2), 3.99(1H, d, J = 5.2 Hz, H-1), 3.77 and 3.66(1H each, dd, H-5,5′), 3.22(1H, q, J = 4.8, 8.7 Hz, H-4), 1.48 and 1.25(3H each, s), 1.03 and 0.82(9H each, s), 0.06 and 0.05(3H each, s). ^{13}C n.m.r. δ 154.9, 135.5, 133.7, 133.0, 129.9, 127.8, 127.4, 119.6, 114.0, 87.5, 81.9, 67.5, 65.6, 63.7, 27.6, 26.5, 25.9, 25.4, 19.5, 18.3, -5.4.

5-*O*-^{t}Butyldimethylsilyl-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-1-(S)-(3-pyridyl)-D-ribitol (12)

A solution of 1,*N*-dehydro-1,4-iminoribitol **3** derived from 0.15 g of iminoribitol **4** was added *via* cannula to a solution of 3-lithiopyridine [prepared by the addition of butyl lithium (1.18 ml, 1.2 M, 1.4 mmol) to a solution of 3-bromopyridine (0.151 ml, 1.57 mmol) in tetrahydrofuran (3 ml) at -100°C and subsequent stirring at this temperature for 0.5 h] at -100°C. The reaction mixture was stirred in the cold bath for 0.5 h and then partitioned between chloroform and water, and the organic phase was dried ($MgSO_4$) and concentrated. Chromatography (ethyl acetate) afforded title compound **12** (0.089 g, 46 %). HRMS calc. for $C_{19}H_{32}N_2O_3Si$: 364.2182; found: 364.2184. ^{1}H n.m.r. ($CDCl_3$) δ 8.58(1H, d, Ar-H), 8.44(1H, m, Ar-H), 7.65(1H, m, Ar-H), 7.17(1H, m, Ar-H), 4.40(1H, dd, J = 4.3, 7.0 Hz, H-3), 4.33(1H, dd, J = 5.3, 7.0 Hz, H-2), 4.11(1H, d, J = 5.3 Hz, H-1), 3.77 and 3.65(1H each, dd, H-5,5′), 3.33-3.28(1H, m, H-4), 1.51 and 1.25(3H each, s), 0.81(9H, s), 0.08, 0.07(3H each, s). ^{13}C n.m.r. δ 148.9, 148.5, 137.0, 134.2, 123.4, 114.2, 87.2, 81.8, 65.9, 65.6, 64.3, 27.6, 25.9, 25.4, 18.3, -5.3.

5-*O*-^{t}Butyldimethylsilyl-1-(S)-(4-carboxyphenyl)-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-D-ribitol (13)

Butyllithium (3.2 ml, 1.3 M, 4.16 mmol) was added dropwise to a solution of 1-(S)-(4-bromophenyl)-5-*O*-^{t}butyldimethylsilyl-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidine-D-ribitol **8** (0.385 g, 0.87 mmol) in tetrahydrofuran (10 ml) at -78°C and the solution was stirred for 1 h at this temperature. Excess solid carbon dioxide was added and the reaction mixture was allowed to warm to room temperature. Acetic acid (2 ml) was added, the solution was partitioned between chloroform and water, the aqueous phase was extracted twice more with chloroform and the combined extracts were dried ($MgSO_4$) and concentrated. Chromatography

(petroleum ether, ethyl acetate 1:1) afforded title compound **13** (0.157 g, 44 %). HRMS (MH^+) calc. for $C_{21}H_{33}NO_5Si$: 407.2128; found: 407.2138. ^1H n.m.r. ($CDCl_3$) δ 7.94 and 7.39(2H each, d, J = 8.3 Hz, Ar-H), 4.52(1H, dd, J = 4.5, 6.9 Hz, H-3), 4.43(1H, t, J = 6.9 Hz, H-2), 4.26(1H, d, J = 5.5 Hz, H-1), 3.83 and 3.74(1H each, dd, H-5,5'), 3.42(1H, q, J = 4.1, 8.0 Hz, H-4), 1.51 and 1.26(3H each, s), 0.81(9H, s), 0.08 and 0.07(3H each, s). ^{13}C n.m.r. δ 170.4, 145.6, 130.4, 129.9, 126.5, 114.5, 87.2, 81.9, 67.3, 65.1, 62.9, 27.6, 25.9, 25.5, 18.3, -5.4.

1-(S)-(3-*N*,*N*-diallylaminophenyl)-*N*-^{t}butoxycarbonyl-5-*O*-^{t}butyldimethylsilyl-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-D-ribitol (14)

1-(S)-(3-*N*,*N*-Diallylaminophenyl)-5-*O*-^{t}butyldimethylsilyl-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-D-ribitol **9** (0.43g, 0.94 mmol) was dissolved in dry dichloromethane (10 ml) and triethylamine (0.39 ml, 2.8 mmol) and di-^{t}butyl carbonate (0.35 g, 1.6 mmol) were added at 0 °C. Stirring was maintained for 1 h at 0 °C and 3 h at room temperature. The excess of di-^{t}butyl carbonate was hydrolysed by the addition of water and the layers were separated. The organic layer was washed twice with aqueous sodium bicarbonate, dried ($MgSO_4$) and evaporated *in vacuo*. Final purification by flash chromatography (petroleum ether, ethyl acetate 10:1) afforded title compound **14** (0.525 g, 99 %) as a colourless syrup: $[\alpha]_D^{20}$ = -10.9 ° (c = 0.65 in CH_2Cl_2), HRMS calc. for $C_{31}H_{50}N_2O_5Si$: 558.3489; found: 558.3474. ^1H n.m.r. (DMSO- d^6, 90°C) δ 7.08 (1H, dd, Ar-H), 6.55 (3H, m, Ar-H), 5.80 (2H, m, CH=), 5.11 (4H, m, $=CH_2$), 4.83 (1H, m, H-3), 4.68 (1H, dd, J = 1.5, 5.8 Hz, H-2), 4.59 (1H, d, J = 5.8 Hz, H-1), 4.01 (1H, q, H-4), 3.87 (4H, m, N-CH_2), 3.73, 3.39 (1H each, dd, H-5,5'), 1.41, 1.27 (3H each, s), 1.31 (9H, s), 0.82 (9H, s), 0.08, 0.07 (3H each, s). ^{13}C n.m.r. δ 155.4, 135.9, 117.3, 112.4, 87.3, 83.1, 80.6, 69.5, 67.2, 64.2, 53.9, 29.3, 28.7, 27.1, 26.8, 18.4, -4.1.

1-(S)-(4-*N*,*N*-diallylaminophenyl)-*N*-^{t}butoxycarbonyl-5-*O*-^{t}butyldimethylsilyl-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-D-ribitol (15)

1-(S)-(4-*N*,*N*-Diallylaminophenyl)-5-*O*-^{t}butyldimethylsilyl-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-D-ribitol **10** (0.37g, 0.8 mmol) was treated as described above for **14**. Final purification by flash chromatography (petroleum ether, ethyl acetate 10:1) afforded title compound **15** (0.45 g, 99 %) as a colourless syrup. $[\alpha]_D^{20}$ = -10.6 ° (c = 2.2 in CH_2Cl_2), HRMS calc. for $C_{31}H_{50}N_2O_5Si$: 558.3489; found: 558.3501. ^1H n.m.r. (d^6 DMSO, 90°C) δ 7.01, 6.61 (2H each, d, Ar-H), 5.80 (2H, m, CH=), 5.11 (4H, m, $=CH_2$), 4.63 (3H, m, H-1,2,3), 3.98 (1H, q, J=4.7, 7.5Hz, H-4), 3.87 (4H, m, N-CH_2), 3.66, 3.48 (1H each, dd, J = 10.2 Hz, H-5,5'), 1.41, 1.27 (3H each, s), 1.31 (9H, s), 0.82 (9H, s), 0.08, 0.07 (3H each,s). ^{13}C n.m.r. δ 155.4, 148.7, 135.9, 129.5, 127.9, 117.3, 113.6, 112.4, 87.0, 82.8, 80.6, 68.5, 67.0, 64.1, 53.9, 29.3, 28.7, 27.1, 26.8, 18.4, -4.1.

1-(S)-(3-Aminophenyl)-*N*-^{t}butoxycarbonyl-5-*O*-^{t}butyldimethylsilyl-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-D-ribitol (16)

1-(S)-(3-*N*,*N*-Diallylaminophenyl)-*N*-^{t}butoxycarbonyl-5-*O*-^{t}butyldimethylsilyl-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-D-ribitol **14** (0.195g, 0.35 mmol) was dissolved in acetonitrile:water (84:16, 40 ml). The reaction mixture was heated to vigorous boiling with a constant argon stream passed through the solution. Tris-triphenylphosphine-rhodium(I) chloride (25 mg) was added and the solvent was distilled off to a cooled (-70 °C) reservoir. The distillation, with constant replacement of the solvent mixture, was continued for 4 h until no starting material could be detected by t.l.c. (petroleum ether, ethyl acetate 1:1). The solvents were evaporated *in vacuo* and the residue was dissolved in ethyl acetate and filtered through silica gel. The solvent was again removed *in vacuo* and the crude product was finally purified by flash chromatography (petroleum ether, ethyl acetate 2:1) to afford title compound **16** (0.112 g, 66 %) as a colourless syrup: $[\alpha]_D^{20}$ = -34.4 ° (c = 0.55 in CH_2Cl_2), HRMS calc. for $C_{25}H_{42}N_2O_5Si$: 478.2863; found: 478.2867. ^{1}H n.m.r. (DMSO- d^6, 90°C) δ 6.94 (1H, dd, Ar-H), 6.43 (3H, m, Ar-H), 4.63 (3H, m, H-1,2,3), 4.03 (1H, q, J = 4.7, 8.3 Hz, H-4), 3.77, 3.49 (1H each, dd, J = 10.1 Hz, H-5,5'), 1.41, 1.27 (3H each, s), 1.31 (9H, s), 0.82 (9H, s), 0.08, 0.07 (3H each, s). ^{13}C n.m.r. δ 155.4, 148.4, 141.7, 128.6, 113.3, 112.9, 112.4, 111.7, 86.1, 81.7, 80.6, 68.1, 65.8, 62.8, 29.3, 28.7, 27.1, 26.8, 18.4, -4.1.

1-(S)-(4-Aminophenyl)-*N*-^{t}butoxycarbonyl-5-*O*-^{t}butyldimethylsilyl-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-D-ribitol (17)

1-(S)-(4-*N*,*N*-Diallylaminophenyl)-*N*-^{t}butoxycarbonyl-5-*O*-^{t}butyldimethylsilyl-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-D-ribitol **15** (0.168 g, 0.3 mmol) was treated as described above for **16**. Final purification by flash chromatography (petroleum ether, ethyl acetate 6:1) afforded title compound **17** (0.094 g, 63 %) as a colourless syrup: $[\alpha]_D^{20}$ = -30.0 ° (c = 0.85 in CH_2Cl_2), HRMS calc. for $C_{25}H_{42}N_2O_5Si$: 478.2863; found: 478.2854. ^{1}H n.m.r. (DMSO- d^6, 90°C) δ 6.87, 6.48 (2H each, d, Ar-H), 4.65 (3H, m, H-1,2,3), 3.95 (1H, q, J = 4.7, 7.7 Hz, H-4), 3.67, 3.47 (1H each, dd, J = 10.2 Hz, H-5,5'), 1.41, 1.27 (3H each, s), 1.31 (9H, s), 0.82 (9H, s), 0.08, 0.07 (3H each, s). ^{13}C n.m.r. δ 155.4, 148.6, 129.4, 127.6, 115.1, 112.4, 87.1, 82.7, 80.6, 68.7, 67.0, 64.0, 29.3, 28.7, 27.1, 26.8, 18.4, -4.1.

***N*-^{t}Butoxycarbonyl-5-*O*-^{t}butyldimethylsilyl-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-1-(S)-(3-nitrophenyl)-D-ribitol (18)**

1-(S)-(3-Aminophenyl)-*N*-^{t}butoxycarbonyl-5-*O*-^{t}butyldimethylsilyl-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-D-ribitol **16** (0.121 g, 0.25 mmol) was dissolved in acetone (10 ml) and aq. sodium bicarbonate solution (10ml) was added. To this mixture a solution of oxone® (0.28 g, 0.45 mmol) in water was added dropwise at 5 °C. Stirring was continued for 1 h at 5 °C and 1 h at r.t. then diethylether (20 ml) was added and

the layers were separated. The aqueous layer was extracted twice with diethylether and the combined organic layers were washed with water and brine, dried over $MgSO_4$ and evaporated *in vacuo*. Final purification by flash chromatography (petroleum ether, ethyl acetate 10:1) afforded title compound **18** (0.103 g, 80 %) as white crystals, mp 93 °C, $[\alpha]_D^{20}$ = -63.3° (c = 0.6 in CH_2Cl_2), HRMS (MH^+) calc. for $C_{25}H_{41}N_2O_7Si$: 509.2683; found: 509.2679. ^1H n.m.r. (DMSO- d^6, 90°C), δ 8.04, 8.11, 7.75, 7.64 (1H each, Ar-H), 4.94 (1H, d, H-3), 4.69 (1H, dd, J = 3.0 Hz, H-2), 4.45 (1H, d, J = 5.4 Hz, H-1), 4.18 (1H, q, J = 4.0, 5.3 Hz, H-4), 3.80, 3.74 (1H each, dd, J = 10.5 Hz, H-5,5'), 1.41, 1.27 (3H each, s), 1.31 (9H, s), 0.82 (9H, s), 0.08, 0.07 (3H each, s). ^{13}C n.m.r. δ 155.4, 148.2, 143.8, 132.4, 129.8, 121.8, 120.5, 112.4, 86.0, 81.5, 80.6, 68.2, 65.5, 63.1, 29.3, 28.7, 27.1, 26.8, 18.4, -4.1.

_N_-^{t}Butoxycarbonyl-5-_O_-^{t}butyldimethylsilyl-1,4-dideoxy-1,4-imino-2,3-_O_-isopropylidene-1-(S)-(4-nitrophenyl)-D-ribitol (19)

1-(S)-(4-Aminophenyl)-_N_-^{t}butoxycarbonyl-5-_O_-^{t}butyldimethylsilyl-1,4-dideoxy-1,4-imino-2,3-_O_-isopropylidene-D-ribitol **17** (0.072 g, 0.15 mmol) was treated as described above for **18**. Final purification by flash chromatography (petroleum ether, ethyl acetate 10:1) afforded title compound **19** (0.056 g, 74 %) as white crystals, mp 69 °C; $[\alpha]_D^{20}$ = -43.4 ° (c = 1.0 in CH_2Cl_2), HRMS (MH^+) calc. for $C_{25}H_{41}N_2O_7Si$: 509.2683; found: 509.2672. ^1H n.m.r. (DMSO- d^6, 90°C) δ 8.17, 7.55 (2H each, d, Ar-H), 4.65 (3H, m, H-1,2,3), 4.15 (1H, q, J = 4.1, 5.6 Hz, H-4), 3.80, 3.73 (1H each, dd, J = 10.3 Hz, H-5,5'), 1.41, 1.27 (3H each, s), 1.31 (9H, s), 0.82 (9H, s), 0.08, 0.07 (3H each, s). ^{13}C n.m.r. δ 155.4, 149.5, 147.0, 127.1, 123.3, 112.4, 85.9, 81.5, 80.6, 68.5, 65.4, 63.0, 29.3, 28.7, 27.1, 26.8, 18.4, -4.1.

1-(S)-(4-Chlorophenyl)-1,4-dideoxy-1,4-imino-D-ribitol (20)

A solution of 5-_O_-^{t}butyldimethylsilyl-1-(S)-(4-chlorophenyl)-1,4-dideoxy-1,4-imino-2,3-_O_-isopropylidene-D-ribitol **6** (0.057 g, 0.146 mmol) in 25 % aq. trifluoroacetic acid (5 ml) was stirred at r.t. for 30 min. Water (20 ml) was added and the aq. layer was washed twice with dichloromethane. The aqueous layer was lyophilised and the residue redissolved in water. The solution was brought to neutral pH by the addition of Amberlyst A-26 ion exchange resin (OH^- form). The resin was filtered off and washed extensively with water and methanol and the solvents were evaporated *in vacuo* and finally removed by freeze drying to yield title compound **20** (0.028 g, 79 %) as a white foam: $[\alpha_D]^{20}$ = -36.2 °(c = 0.65 in H_2O), HRMS calc. for $C_{11}H_{14}NO_3Cl$: 243.0662, found: 243.0660. ^1H n.m.r. (D_2O) δ 7.37 (4H, m, Ar-H), 3.98 (3H, m, H-1,2,3), 3.70, 3.66 (1H each, dd, J = 10.5 Hz, H-5,5'), 3.15 (1H, ddd, J = 3.5, 5.3, 5.5 Hz, H-4). ^{13}C n.m.r. δ 140.8, 135.6, 131.5, 131.3, 79.2, 74.7, 67.4, 67.3, 64.9.

1,4-Dideoxy-1-(S)-(4-fluorophenyl)-1,4-imino-D-ribitol (21)

A solution of 5-*O*-^{t}butyldimethylsilyl-1,4-dideoxy-1-(S)-(4-fluorophenyl)-1,4-imino-2,3-*O*-isopropylidene-D-ribitol **7** (0.090 g, 0.23 mmol) in 50 % aqueous trifluoroacetic acid was allowed to stand at room temperature for 3h and then concentrated to dryness. The residue was dissolved in water, washed with dichloromethane, and then the aqueous phase was evaporated. The residue was redissolved in water and the solution was neutralised with Amberlyst A 26 ion exchange resin (OH^- form), the resin was filtered off and washed liberally with methanol. The filtrate was concentrated and finally lyophilised to give title compound **21** (0.024 g, 45 %). HRMS calc. for $C_{11}H_{14}FNO_3$: 227.0958; found: 227.0960. ^{1}H n.m.r. (D_2O) δ 7.44(2H, dd, J = 5.5, 8.6 Hz, Ar-H), 7.17(2H, t, J = 8.8 Hz, Ar-H), 4.09(3H, br s, H-1,2,3), 3.76(2H, d, H-5,5′), 3.26(1H, q, J = 5.1, 8.7 Hz, H-4). ^{13}C n.m.r. δ 165.2(d, $J_{C,F}$ = 244 Hz), 137.4, 132.1(d, $J_{C,F}$ = 8.1 Hz), 118.4(d, $J_{C,F}$ = 21.5 Hz), 79.1, 74.8, 67.8, 67.4, 64.7.

1-(S)-(4-Bromophenyl)-1,4-dideoxy-1,4-imino-D-ribitol (22)

1-(S)-(4-Bromophenyl)-5-*O*-^{t}butyldimethylsilyl-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-D-ribitol **8** (0.10 g, 0.22 mmol) was treated as described above for the preparation of **21** to give title compound **22** (0.017 g, 26 %). HRMS calc. for $C_{11}H_{14}{}^{79}BrNO_3$: 287.0157; found: 287.0156. ^{1}H n.m.r. (D_2O) δ 7.58 and 7.34(2H each, d, J = 8.4 Hz, Ar-H), 4.08-3.97(3H, m, H-1,2,3), 3.74(2H, m, H-5,5′), 3.19(1H, q, J = 5.1, 8.9 Hz, H-4). ^{13}C n.m.r. δ 141.7, 134.5, 132.0, 124.0, 79.4, 74.9, 67.7, 67.6, 65.1.

1,4-Dideoxy-1-(S)-(4-hydroxyphenyl)-1,4-imino-D-ribitol (23)

A solution of 5-*O*-^{t}butyldimethylsilyl-1-(S)-(4-^{t}butyldiphenylsiloxyphenyl)-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-D-ribitol **11** (0.20 g, 0.32 mmol) in 50 % aqueous trifluoroacetic acid (10 ml) was allowed to stand at room temperature for 16 h and then the solution was evaporated. The residue was dissolved in water, extracted with dichloromethane (x2), and the aqueous phase was concentrated. The residue was again dissolved in water, stirred with Amberlyst A 21 ion exchange resin (1 g) for 0.5 h, and then the solids and solvent were removed. The product was further purified by chromatography (CH_2Cl_2, MeOH 3:1) affording title compound **23** (0.061 g, 83 %). HRMS calc. for $C_{11}H_{15}NO_4$: 225.1001; found: 225.0999. ^{1}H n.m.r. (D_2O) δ 7.36 and 6.95(2H each, d, J = 8.6 Hz, Ar-H), 4.34-4.18(3H, m, H-1,2,3), 3.83(2H, d, J = 5.1 Hz, H-5,5′), 3.47(1H, q, J = 4.9, 9.0 Hz, H-4). ^{13}C n.m.r. δ 158.8, 132.1, 129.9, 118.5, 77.6, 74.1, 67.8, 67.0, 63.2.

1,4-Dideoxy-1,4-imino-1-(S)-(3-pyridyl)-D-ribitol (24)

5-*O*-^{t}Butyldimethylsilyl-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-1-(S)-(3-pyridyl)-D-ribitol **12** (0.089 g, 0.24 mmol) was treated as described above in the preparation of **23** affording title compound **24** (0.031 g, 60 %). HRMS calc. for $C_{10}H_{14}N_2O_3$: 210.1004; found: 210.1002. ^{1}H n.m.r. (D_2O) δ 8.54(1H, s, Ar-H), 8.47(1H,

d, J = 4.9 Hz, Ar-H), 7.91(1H, d, J = 8.0 Hz, Ar-H), 7.47(1H, dd, J = 4.9, 8.0 Hz, Ar-H), 4.09-4.05(3H, m, H-1,2,3), 3.77-3.68(2H, m, H-5,5'), 3.25(1H, q, J = 5.4, 9.1 Hz, H-4). ^{13}C n.m.r. δ 151.1, 150.7, 139.0, 138.8, 127.3, 79.3, 74.9, 67.8, 65.8, 65.4.

1,4-Dideoxy-1,4-imino-1-(S)-(3-nitrophenyl)-D-ribitol (25)

A solution of *N*-^{t}butoxycarbonyl-5-*O*-^{t}butyldimethylsilyl-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-1-(S)-(3-nitrophenyl)-D-ribitol **18** (0.058 g, 0.114 mmol) in methanol and 3M aqueous HCl (10 ml, 1:1) was allowed to stand at room temperature for 3 h. The methanol was removed *in vacuo* and the aqueous solution was washed twice with dichloromethane. The resulting solution was lyophilised and the residue was redissolved in water/methanol (5 ml, 1:1) and neutralised with Amberlyst A 26 ion exchange resin (OH^- form). The resin was filtered and washed extensively with water and then methanol. The solvents were evaporated *in vacuo* and finally lyophilised to yield title compound **25** (0.024 g, 82 %) as a colourless foam: $[\alpha_D]^{20}$ = -24.0 ° (c = 0.2 in MeOH), HRMS (MH^+) calc. for $C_{11}H_{15}N_2O_5$: 255.0981; found: 255.0985. ^{1}H n.m.r. (d^4 MeOH) δ 8.39, 8.26, 7.80, 7.48 (1H each, Ar-H), 4.09 (1H, d, J = 7.5 Hz, H-1), 3.84 (1H, m, H-3), 3.68 (1H, dd, J = 5.8 Hz, H-2), 3.61, 3.56 (1H each, dd, J = 5.0, 11.2 Hz, H-5,5'), 3.28 (1H, m, H-4). ^{13}C n.m.r. δ 149.7, 146.0, 134.6, 130.4, 123.1, 122.8, 79.4, 73.6, 66.7, 66.5, 64.6.

1,4-Dideoxy-1,4-imino-1-(S)-(4-nitrophenyl)-D-ribitol (26)

N-^{t}Butoxycarbonyl-5-*O*-^{t}butyldimethylsilyl-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-1-(S)-(4-nitrophenyl)-D-ribitol **19** (0.042 g, 0.083 mmol) was treated as described above for **25** to give title compound **26** (0.015 g, 71 %) as a light yellow foam: $[\alpha_D]^{20}$ = -29.5 ° (c = 0.2 in MeOH), HRMS (MH^+) calc. for $C_{11}H_{15}N_2O_5$: 255.0981; found: 255.0993. ^{1}H n.m.r. (MeOH- d^4) δ 8.13, 7.64 (2H each, d, Ar-H), 4.18 (1H, d, J = 7.4 Hz, H-1), 3.88 (1H, dd, J = 5.8, J = 4.0 Hz, H-3), 3.80 (1H, dd, H-2), 3.63 (2H, AB, H-5,5'), 3.22 (1H, m, H-4). ^{13}C n.m.r. δ 151.2, 148.7, 129.3, 124.5, 79.5, 73.7, 66.8, 66.8, 64.4.

1-(S)-(4-Carboxyphenyl)-1,4-dideoxy-1,4-imino-D-ribitol ammonium salt (27)

A solution of 5-*O*-^{t}butyldimethylsilyl-1-(S)-(4-carboxyphenyl)-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-D-ribitol **13** (0.160 g, 0.39 mmol) in 50 % aqueous trifluoroacetic acid was allowed to stand at room temperature for 4 h and then concentrated to dryness. The residue, in water, was washed with dichloromethane (x2) and then the aqueous phase was filtered and concentrated. This residue was dissolved in water and applied to a small column of Amberlyst A 15 ion exchange resin (H^+ form, 1.25g). The resin was eluted with water (10 ml), which was discarded. Further elution with 2 M aqueous ammonia (20 ml) afforded, after lyophilisation, title compound **27** (0.076 g, 71 %). ^{1}H n.m.r. (D_2O) δ 7.79 and 7.46(2H each, d, J = 7.9 Hz, Ar-H), 4.38(2H, bs), 4.20(1H, bs), 3.83(2H, bs), 3.55(1H, m). ^{13}C n.m.r. δ 177.7, 140.4, 139.7, 132.2, 130.4, 77.6, 74.1, 68.2, 67.1, 62.9.

1-(S)-(3-Aminophenyl)-5-*O*-^{t}butyldimethylsilyl-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-D-ribitol (28).

1-(S)-(3-*N*,*N*-Diallylaminophenyl)-5-*O*-^{t}butyldimethylsilyl-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-D-ribitol **9** (0.260 g, 0.56 mmol) was treated as described above for **16** and the crude product was purified by flash chromatography (petroleum ether, ethyl acetate 2:1) to afford pure **28** as a light yellow syrup (0.127 g, 61 %). $[\alpha]_D^{20}$ = -18.8° (c = 0.95 in CH_2Cl_2), HRMS calc. for $C_{20}H_{34}N_2O_3Si$: 378.2338; found: 378.2333. ^{1}H n.m.r. ($CDCl_3$) δ 7.03, 6.68, 6.53, 6.49 (1H each, Ar-H), 4.39 (1H, dd, J = 4.6, 7.0 Hz, H-3), 4.33 (1H, dd, H-2), 4.01 (1H, d, J = 5.0 Hz, H-1), 3.78, 3.67 (1H each, dd, J = 10.2 Hz, H-5,5'), 3.22 (1H, q, J = 3.7, 5.3 Hz, H-4), 1.49, 1.25 (3H each, s), 0.82 (9H, s), 0.08, 0.07 (3H each, s). ^{13}C n.m.r. δ 146.4, 142.5, 129.7, 116.4, 113.9, 113.0, 87.4, 81.6, 67.6, 65.4, 63.5, 27.5, 25.9, 25.4, 18.3, -5.4.

1-(S)-(4-Aminophenyl)-5-*O*-^{t}butyldimethylsilyl-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-D-ribitol (29)

1-(S)-(4-*N*,*N*-Diallylaminophenyl)-5-*O*-^{t}butyldimethylsilyl-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-D-ribitol **10** (0.242 g, 0.52 mmol) was treated as described above for **28** to yield title compound **29** (0.131 g, 67 %) as a light yellow syrup: $[\alpha]_D^{20}$ = -22.0 ° (c = 0.85 in CH_2Cl_2), HRMS calc. for $C_{20}H_{34}N_2O_3Si$: 378.2338; found: 378.2330. ^{1}H n.m.r. ($CDCl_3$) δ 7.09, 6.56 (2H each, d, J = 8.1 Hz, Ar-H), 4.42 (1H, dd, J = 4.8, 7.0Hz, H-3), 4.33 (1H, dd, H-2), 3.99 (1H, d, J = 5.1 Hz, H-1), 3.78, 3.68 (1H each, dd, J = 10.2 Hz, H-5,5'), 3.21 (1H, q, J = 3.6, 5.0 Hz, H-4), 1.49, 1.25 (3H each, s), 0.82 (9H, s), 0.08, 0.07 (3H each, s). ^{13}C n.m.r. δ 145.5, 131.1, 127.4, 114.9, 113.9, 87.6, 81.7, 67.4, 65.4, 63.4, 27.5, 25.9, 25.4, 18.3, -5.4.

1-(S)-(3-Aminophenyl)-1,4-dideoxy-1,4-imino-D-ribitol (30).

1-(S)-(3-Aminophenyl)-5-*O*-^{t}butyldimethylsilyl-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-D-ribitol **28** (0.068 g, 0.18 mmol) was treated as described above for **20** to yield title compound **30** (0.026 g, 67 %) as a white foam, $[\alpha_D]^{20}$ = -34.9 °(c = 0.4 in H_2O). HRMS calc. for $C_{11}H_{16}N_2O_3$: 224.1160; found: 224.1161. ^{1}H n.m.r. (D_2O) δ 7.13 (1H, dd, Ar-H), 6.70 (3H, m, Ar-H), 3.92 (2H, m, H-1,3), 3.82 (1H, dd, J = 3.8, J = 7.5 Hz, H-2), 3.66, 3.62 (1H each, dd, J = 12.5 Hz, H-5,5'), 3.07 (1H, q, J = 5.0 Hz, H-4). ^{13}C n.m.r. δ 149.4, 143.4, 132.6, 120.8, 118.7, 117.6, 79.3, 74.9, 68.3, 67.5, 64.7.

1-(S)-(4-Aminophenyl)-1,4-dideoxy-1,4-imino-D-ribitol (31)

1-(S)-(4-Aminophenyl)-5-*O*-^{t}butyldimethylsilyl-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-D-ribitol **29** (0.107 g, 0.28 mmol) was treated as described above for **20** to yield title compound **31** (0.053 g, 84 %) as a white solid with mp 166 °C, $[\alpha_D]^{20}$ = -44 °(c = 0.55 in H_2O). HRMS calc. for $C_{11}H_{16}N_2O_3$: 224.1160; found:

224.1160. ^{1}H n.m.r. (D_2O) δ 7.21, 6.80 (2H each, d, Ar-H), 4.19 (1H, dd, J = 8.5, J = 5.5 Hz, H-3), 4.08 (2H, m, H-1,2), 3.75 (2H, AB, H-5,5'), 3.33 (1H, q, H-4). ^{13}C n.m.r. δ 149.6, 131.6, 129.5, 119.3, 77.9, 74.1, 67.7, 67.4, 63.5.

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